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INVITED COMMENTARY

Commentary on: "White Matter Damage of the Brain is Associated With Poor Outcomes in Vascular Surgery Patients with Claudication: A Pilot Study"

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Changes in cerebral white matter can be investigated using newer MRI-diffusion technologies. In the current issue of the *European Journal of Vascular and Endovascular Surgery*, a pilot study reports on the association between peripheral arterial disease (PAD) and white matter changes in the brain using MRI-diffusion imaging and calculation of fractional anisotropy.[1] The study reports a reduction in the fractional anisotropy scale in patients with PAD, especially those suffering fatal or severe cardiovascular events during follow up. This is a new finding, which is worthy of further evaluation. In particular, such complex measurements need to be validated regarding inter-individual and inter-observer variability: is the anisotropy value the same in the morning as in the evening?

Water diffusion displays directionality because of the presence of complex microstructural barriers in tissue. The extent of directionality of water diffusion can be expressed as fractional anisotropy, but what does this actually mean, and how is it calculated? It has been speculated to reflect fiber density, axonal diameter, myelination in white matter and metabolism. The current pilot study showing this new association is small, and its results must, therefore, be validated in larger prospective studies (as was stated by the authors). However, a study like this actually raises more questions than it answers: How does fractional anisotropy develop differently in patients with PAD compared to the changes observed in an ageing human? Are the white matter changes in aorto-iliac atherosclerosis different from those in patients with distal atherosclerotic lesions (hard to differentiate in the current study)? Is there a difference between claudicants and those with critical ischemia (only one patient with critical ischemia was included in the pilot study)? Is there a difference in diabetic patients (nine patients with diabetes showed no difference in the pilot study)? Is abnormal fractional anisotropy related to the later development of cerebral small vessel disease and lacunar infarcts? In the pilot study seven cardiac events and one stroke were reported.

The authors speculate that the reduction in fractional anisotropy in patients with PAD could represent loss of micro-integrity and metabolic or inflammatory changes in the white matter. For lacunar disease, elevated homocysteine, cholesterol, and inflammatory levels have previously been noted. If the pilot study findings are validated in future studies, it might be possible to develop a better understanding of what is represented by these white matter changes. Perhaps even pharmacological interventions could be monitored by this new technique? Does reduced fractional anisotropy really matter? Only time will tell.

REFERENCE

1 Virtanen S, Utriainen KT, Parkkola R, Airaksinen JK, Laitio R, Scheinin H, et al. White matter damage of the brain is associated with poor outcome in vascular surgery patients with claudication: a pilot study. *Eur J Vasc Endovasc Surg* 2014;**48**:687–93.

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